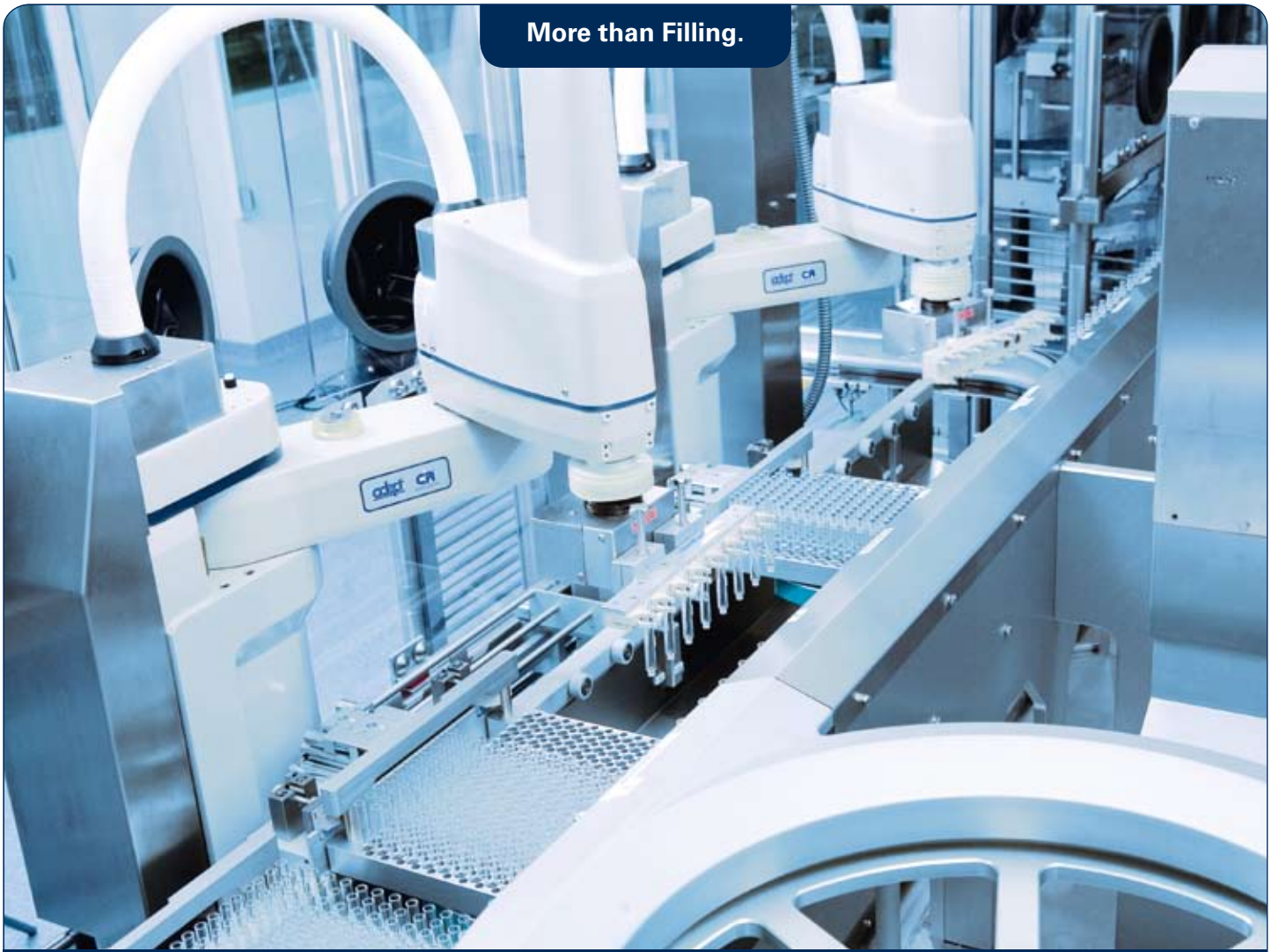


More than Filling.



## Vetter White Paper Edition

### **Finding the right contract manufacturer**

Vetter Pharma International GmbH



Pharma solutions for tomorrow, today.

## Introduction

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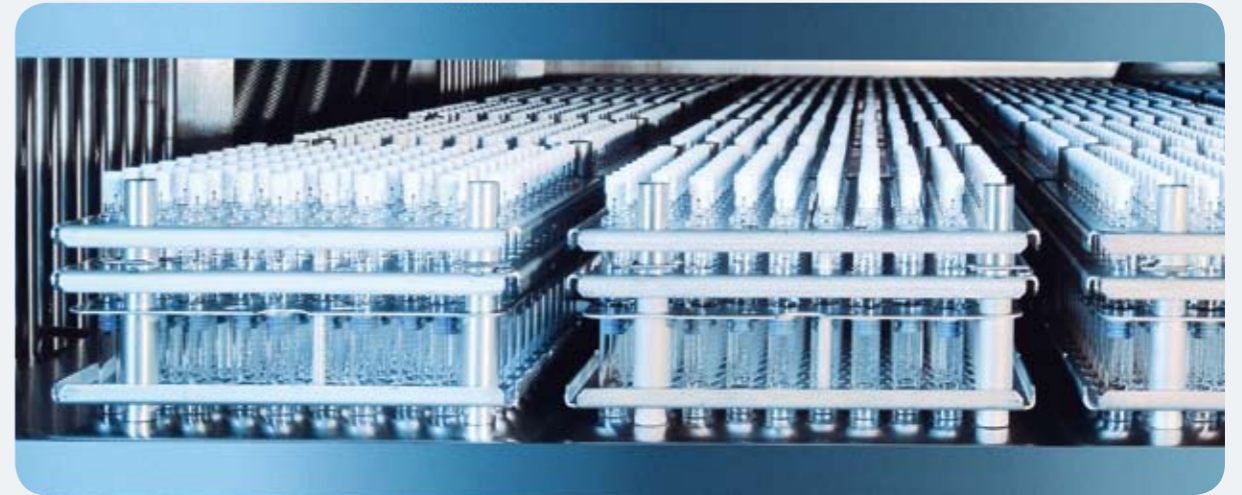
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Contract manufacturing became popular in many industries during the 1990s as a way to counter rising costs and to reinvestment. The pharmaceutical industry has been slow to adopt this practice because of its absolute need for secrecy.

However, with fewer blockbuster drugs in the pipeline, companies are on the lookout for an enduring solution to meet market challenges. These include rising process costs resulting from stricter quality control criteria, evolving technologies, which are becoming more complex and costly, and the increasing stringency of regulatory standards. To maintain or expand market shares, pharmaceutical companies must devise new strategies to remain competitive.

## Finding the right contract manufacturer



**Finding a suitable contract manufacturer is,** perhaps, one of the most viable options. The pharmaceutical company can concentrate effort and money on research and development and marketing, while the contract manufacturer takes care of the manufacturing process, including validation, support for license application and packaging. In addition, outsourcing can be scheduled into the strategic planning of a drug's lifecycle. During the early development phases, which last years, a partner with the necessary facilities and experience can be sought out and brought onboard. Finding the proper partner requires careful screening, hence a certain amount of time. A number of criteria should be met. The first is simply know-how and experience: How long has a contract manufacturer been in the business and what kind of work has the company done, i.e. with what kind of drugs. The more experience, the smoother the collaboration. Finally, to ensure effective workings, outsourcing has to be made an integral aspect of project management.

**The manufacturing processes** involved in filling syringes, vials and cartridges is one of the most complex and difficult procedures in the pharmaceutical world and serves as an excellent example of what might be needed for a successful partnership. If a company is intending to put a parenteral drug on the market, then, the entire manufacturing process in fact becomes the best candidate for outsourcing, since it is very costly, involves an extremely wide range of procedures and needs a lot of experience. It involves such steps as matching the product's active substance with its mode of administration, process development and transfer to commercial manufacturing. There are several keys to success: including the requirements for the future commercial manufacturing in the initial development phase, and having a precise project plan, competent project management and an effective filing strategy in order to speed up time to market.

## The basics

**Most pharmaceutical companies**, but especially the smaller biotech firms that produce niche drugs, will not have the capacity nor the financial strength to maintain, much less build, any capacities for manufacturing. This is especially true in light of the regulatory constraints. While the only real alternative is indeed using the services of a contract manufacturer, a drug company cannot just look one up in the phone book and take the first one, of course. The candidate will have to fulfil a number of important criteria, including a sound expertise of aseptic filling from development to commercial manufacturing, an extensive knowledge of validation procedures, an excellent relationship with regulators, and even a knowledge of marketing.

### So: what makes a good contract manufacturer?

It does not suffice to have a few filling lines. The facility itself must be "state-of-the-art" these days, in order to provide the highest quality product, which in turn will facilitate validation. It will need sophisticated laboratories and an elaborate concept for cleanrooms. Having up-to-date technology for performing aseptic filling, such as lines equipped with a Restricted Access Barrier System, is an advantage for several reasons. The technology itself is the safest available and it gives the company a great deal of flexibility in filling. This shows that the contract manufacturer is very much on the front lines of innovation in the business.

**The contract manufacturer** must also have sufficient capacity in order to absorb a possible surge in demand. The company in question must have a proper back-up concept as well to cover a host of scenarios from a common power failure and other possible events. In real terms, filling facilities must be equipped with an effective back-up power supply, a reliable supply of spare parts, in-house engineering capabilities, media

supplies, and so on. A very conscientious contract manufacturer might even have more than one supplier, in case one cannot deliver for some reason. Furthermore, having additional filling lines does not suffice for total reliability: Back-up filling lines must be at another location several miles away in the event of a catastrophic event.



## The portfolio factor

If a company has the capacity and the safety through back-up systems, it is important to find out what kind of services and solutions the potential contract manufacturer has available. When it comes to services, for example, one must see to what extent they are integrated into a larger concept. The most efficient option is a program of services that starts with the support in product development and takes the lifecycle management of the drug to be filled into consideration. The contract manufacturer will ideally be able to offer various options in primary and secondary packaging. Properly planned, this can also considerably reduce time to market of a drug. This is another area where the contract manufacturer can take some of the burden off the drug manufacturer.

The availability portfolio of solutions is critical. A contract manufacturer with a full range of products will have the necessary flexibility to address the needs of

the market. A basic portfolio should include single chamber syringes, vials and cartridges. Any additional, innovative products will also represent a plus factor. These might include special solutions, tracking systems that a product can be traced from the filling line to the patient, and tamper-evident solutions. These are especially important when it comes to another vital aspect of filling mentioned above, namely life-cycle management. If a lyophilized drug is to hit the market fast in a first cycle, it will probably be in a vial. For the second cycle – depending on the drug – the drug company may opt for a more patient-friendly form like a dual-chamber syringe or cartridge. A viable contract manufacturer will have these capabilities on hand. Lifecycle management is an aspect that should not be underestimated: if planned early enough, it can mean the real success of a drug against up-coming competition.

## Finances: for the long term



The other soft factor that needs to be investigated carefully is the financial stability of a potential contract manufacturer – a subject that is related in some ways to the need for back-up. Manufacturing a drug is not only a one-shot event, nor is it a brief one. In a best-case scenario, a drug can take less than 12 months from first feasibility, process development to commercial manufacturing. In other words, a drug company is looking at a long-term relationship with the contract manufacturer, which should be able to show that it has the independent financial standing power. A contract manufacturer with a history of organic, consistent growth will prove to be a strong ally, generally.

## Looking at the soft factors

Assuming a candidate company fulfils all of the “hard” criteria there remains a number of other areas to review. Actual know-how and experience in manufacturing must be just as up-to-date as the facilities. Having well trained teams of scientists and engineers is a must. It is one way to ensure a competent and creative approach to solving problems that might arise. It can also contribute to speeding up time-to-market. A well-versed team can work more efficiently, since they will have comprehensive checklists for all processes and can organize each and every element so that no time is wasted.

Another criterion for a good contract manufacturer is the company’s actual market scope. How positioned is it internationally? The pharmaceutical industry in each country has its own regulatory systems and its

own national specifications. But if a contract manufacturer has already filed for drugs that are sold globally, it is safe to assume that it has developed a significant body of experience that will have been integrated in its processes. Furthermore, it will already have established a solid working relationship with regulatory authorities that can save a lot of time and effort when it comes to validation and seeking approvals. Having documented approvals by international regulatory agencies such as the Food and Drug Administration (FDA), the EMEA and other authorities is essential, in particular if a drug company is trying to reach an international market. It is just one more element in chipping away at time to market, which can save a drug company a great deal amount of money.

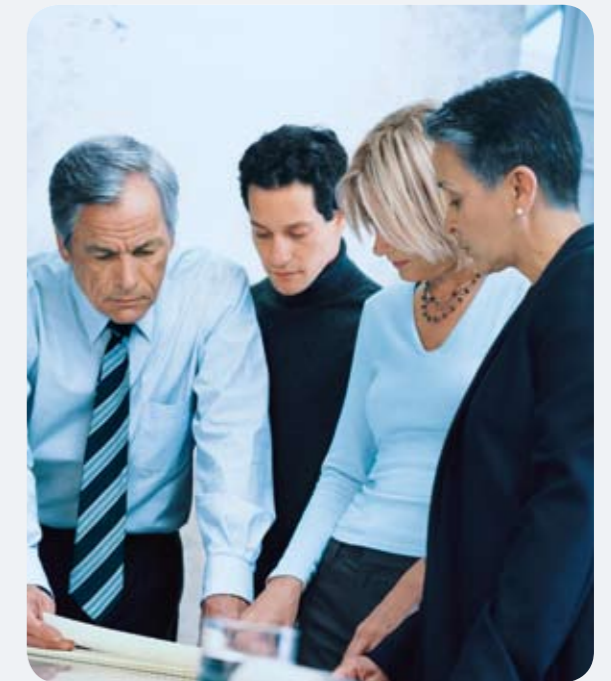
## The benefits of partnership

Manufacturing drugs, especially new, innovative, “high-tech” substances, involves considerable risks, first and foremost financial: Will the drug be a success or not? Establishing a productive and balanced relationship with a contract manufacturer means sharing possible risks. It involves regulating scenarios in the event of a boom, or, should the product encounter problems, slowing or even halting production. In addition, no company can say for sure whether their newest product will achieve a breakthrough on the market or when, building filling lines would be relevant. The contract manufacturer will have the experience, which further reduces expenses by shortening the famous learning curve, the time spent with trial and error activities. Once the product is launched, the contractor will then be responsible for harmonising production and demand.



## Working together

Adopting a sustainable outsourcing strategy can lead to a perfect win-win situation. But it also requires an investment on the part of both parties. A contract manufacturer will want to have the experience in such partnerships and be flexible and innovative. Integrated management is required to make sure each project is being handled properly and communication channels are open. Regular planning sessions must be held to ensure that each party is fully informed of any potential roadblocks. All processes carried out by all parties involved must be carefully documented for future reference. In fact, the best way to keep track of a project’s progress is to jointly establish performance measures that can be easily quantified using objective data. These are simply best practices. Ultimately, however, a company seeking to outsource production processes will be dependent on its partner, to a certain extent. Confidential information and knowledge is shared. In the end, therefore, the true core of any partnership is trust.



## A partnership for success

In the future, outsourcing certain processes will become an important strategy in the pharmaceutical industry to meet the growing number of challenges. Experience has shown that outsourcing is not really profitable in the short-term, however, unless necessitated by an emergency of course. The relationship should be long-term since – as suggested above – it will also influence the future lifecycles of a drug and requires investments of time and money. It is a fundamental decision that must be made in the early phases of a drug’s development, when time is sufficient to find the perfect partner and develop a strong relationship. For a drug company facing the pressures of today’s markets,

having a committed ally can make all the difference. A good contract manufacturer will be there throughout all stages of a drug’s development and through all the lifecycles, providing the necessary support at all times. This will provide the pharmaceutical company with valuable time and resources to concentrate on its core activities, namely research and development into other drugs and marketing. It’s a win-win situation bound to provide market success.

**More than Filling.**

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